

Going After Lipotoxins to Reduce Inflammation in the Airway of Cystic Fibrosis Patients

Saeed S. Akhand¹, Gregory G. Anderson¹

Department of Biology, Indiana University Purdue University Indianapolis.

People with cystic fibrosis (CF) typically have chronic lung infections, predominantly with *Pseudomonas aeruginosa*. Lung inflammation, in connection with bacterial colonization, is one of the major factors contributing to the morbidity and mortality of CF patients. Recent studies suggest that a common mutation among CF *P. aeruginosa* isolates (in the gene *mucA*) results in high-level expression of lipoproteins which stimulates a pro-inflammatory reaction in cultured CF-derived airways cell (CFBE). Our previous work in this area has revealed that a strain containing a mutation in the putative lipotoxin gene *PA4326* is dramatically less toxic to CFBE. We hypothesize that lipotoxins lead to airway structure damage by causing epithelial cell death and tissue destruction, possibly as a downstream effect of immune stimulation. Our results demonstrate that deletion of the *PA4326* gene does not affect growth, motility, adhesion, or biofilm development. However, this mutant strain produces 59.1% less pyocyanin compared to the non-mutant strain. Pyocyanin is a bacterial toxin that triggers airway inflammation by stimulating the immune system to produce the signaling molecule IL-8. Thus, our data suggest a possible clue about the decreased toxicity of the *PA4325* mutant. The aim of future work is to confirm the role of this lipotoxin gene in the inflammatory process and to elucidate the underlying mechanism of its function. Our long term goal is to characterize other lipotoxins and to develop a novel inhibitor of *lspA* (a bacterial gene required for lipotoxin production) as an anti-inflammatory strategy to slow down the airway damage and hence improve the longevity and quality of life for people with CF.

Advisor: Gregory G. Anderson, Department of Biology, Indiana University Purdue University Indianapolis